

### REMARKS

Claims 12, 18-21, 29 and 34-43 are pending. Claims 34 and 40-42 have been withdrawn from consideration. Claims 12, 18-21, 29, 35-39 and 43 are rejected. Claim 38 has been amended to encompass additional subject matter the applicant believes it is entitled to claim. No new matter has been added.

#### **1. Election/Restriction**

The Examiner expresses some confusion regarding the applicant's previous statement that claim 38 is generic to the elected species. Claim 38 has been amended to recite that substituents  $R^9$ ,  $R^{10}$  and  $R^{11}$  can be hydrogen, provided that substituents  $R^{10}$  and  $R^{11}$  are not both hydrogen. Support for the amendment can be found, *inter alia*, at pages 29-36, 41, and 42 of the specification (specifically, in Tables VI and VII, and Examples 1-3, 5-7, 9, and 21-23).

As amended, claim 38 is directed to a combinatorial library that includes a plurality of  $\beta,\gamma$ -unsaturated- $\alpha$ -amino acid derivatives of formula 23. The applicant submits that the claim, as amended, is generic to the elected species, in that the claim encompasses the elected species -- that is, a combinatorial library of  $\alpha$ -amino acids having a core framework of structure 1 and wherein the carbonyl component (the compound of formula 14) is glyoxylic acid (HCOCOOH), and including at least the compounds prepared in Examples 1, 2, 3, 6, 8, 9, 10, 11, 12, 14, 15, 18, 22, 23, 24 and 25 (of which multiple compounds are  $\beta,\gamma$ -unsaturated- $\alpha$ -amino acid derivatives that satisfy formula 23) -- although the claim does cover combinatorial libraries other than the elected library as well. The applicant respectfully submits that it understood the Examiner's Election of Species requirement to require the applicant to identify a species of library including specific compounds for purposes of the Examiner's search, but that a "species" commensurate in scope with claim 38 is acceptable if that satisfies the Examiner's request.

#### **2. Information Disclosure Statement**

As requested, the applicant is resubmitting copies of the documents cited in the IDS filed on June 1, 2001 for the Examiner's convenience.

#### **3. Rejections under Section 112**

Claims 12, 18-21, 29, 35-39 and 43 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to reasonably convey that the inventors had possession of the invention at the time the application was filed. The applicant respectfully disagrees.

The Examiner states that the application does not describe the combinatorial libraries recited in the present claims, asserting that the application includes "only a vague showing that they (the combinatorial libraries) were even contemplated in the generic sense", citing the specification's definition of "combinatorial library" at lines 14-36 of the specification. Office Action, page 4.

The applicant submits that this disregards numerous statements in the specification that clearly demonstrate that combinatorial libraries, including the libraries recited in the instant claims, fall squarely within the scope of the invention contemplated by the inventors at the time of filing. Thus, for example, in the first description of the invention under the headings "General Description: Synthesis of amines", the specification states that "One aspect of the invention is a process for generating a combinatorial library consisting of compounds of formula 1, by combining compounds 13, 14 and 15". Specification, page 8, lines 9-11. As both the "Summary of the Invention" and original claims make clear, the inventors clearly contemplated that such combinatorial libraries were within the scope of their invention: "Another aspect of the invention is a combinatorial library generated through the process of the invention." *Id.* at page 6, lines 23-24; *see also* page 56, lines 6-7 (original claim 12).

As the definition cited by the Examiner states, the specification uses the term "combinatorial library" to refer to "a set of compounds that are made by the same process, by varying one or more of the reagents." *Id.* at page 7, lines 14-16. With reference to the process described on page 8 (which, in combination with the process described on page 9 corresponds directly to the process recited in claim 12), the specification recites that "[t]he multicomponent nature of the process described in this invention allows the direct and rapid generation of combinatorial libraries of the products, by varying the desired substituents." *Id.* at page 9, lines 6-8. Both the definition and detailed description note that the combinatorial libraries can be made as individual pure compounds or as mixtures of compounds, and describe libraries formed

by holding one component constant and varying the identity of the other components across multiple compounds in the library. *Id.* at page 7, lines 16-35; page 9, lines 9-19.

The applicant submits that this disclosure clearly demonstrates the inventors' possession of the subject matter of the instant claims at the time the application was filed. Claim 12 is directed to a combinatorial library including a plurality of compounds, in which a plurality of the compounds in the library are prepared by a process in which an amine, carbonyl, and organoboron compound are mixed and allowed to react to form a compound in the combinatorial library. Claim 18 depends from claim 12 and further specifies the structure of a plurality of compounds of the combinatorial library recited in claim 12, which structure is precisely the structure of the product, compound 1, of the process described on page 8 of the specification. Similarly, claim 19 depends from claim 12 and specifies that the combinatorial library is prepared by varying the amine, carbonyl, and organoboron components used to generate a plurality of compounds of formula 1. Claims 20 and 21 are directed to different formats of libraries, claim 20 reciting a library that contains a mixture of different compounds of formula 1, and claim 21 reciting a library of individual compounds located at different positions in an array. The applicant submits that all of these claims clearly fall squarely within the express disclosure discussed above.

Claims 29, 35-39 and 43 are directed to more specific embodiments of the invention that are also expressly described in the specification. Thus, claim 29 recites that the components from which the library compounds are formed are mixed in the presence of air. *See id.* at page 21, lines 9-11. Claim 35 recites the use of chiral components in the stereoselective production of reaction products. *See, e.g., id.* at page 10, lines 25-32; page 21, lines 12-16; page 22, lines 26-28 & Tables III, IV, VI & VII. Claim 36 recites the further transformation of the compounds. *See, e.g., id.* page 9, lines 1-5. Claim 37 recites that a plurality of compounds in the combinatorial library are amino acids (which amino acids fall within the scope of formula 1). *See, e.g., id.* at page 5, lines 21-27; page 10, lines 13-32; page 12, lines 8-21. Claim 38 recites a particular class of amino acids, the  $\beta,\gamma$ -unsaturated- $\alpha$ -amino acid derivatives of formula 23, which the specification describes as being particularly suited to the techniques of the invention. *See id.* at page 12, line 22-page 14, line 25. Claim 39 recites the more general class of  $\alpha$ -amino

carbonyl derivatives. *See, e.g., id.* at page 13, line 34-page 17, line 2. Finally, claim 43 recites that at least one of the amine, carbonyl or organoboron components is attached to a solid support. *See, e.g., id.* at page 9, lines 9-17. The applicant submits that each of these claims is fully supported by at least the exemplary supporting disclosure cited above, and requests that the rejections under section 112 be withdrawn.

#### 4. Rejections under Sections 102 and 103

Claims 12, 18-21, 29, 35-39 and 43 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by or, in the alternative, under 35 U.S.C. § 103 as allegedly being obvious over U.S. Patent No. 4,421,767 ("Palfreyman"). The applicant respectfully disagrees.

The Examiner states that Palfreyman "discloses collections of compounds (reading on the claimed 'combinatorial library') that read directly on the instant formulas 1 and 23." Office Action, page 6. Pointing to particular molecular formulas disclosed in Palfreyman, the Examiner states that "The collections of compounds of the reference reads (sic) on applicant's definition of 'combinatorial library' (see, instant specification, page 7, lines 14-36)."

Nowhere, however, does Palfreyman appear to disclose combinatorial libraries of its compounds as each of the applicant's current claims require. As noted above, the applicant's specification defines "combinatorial library" to mean "a set of compounds" made by the same process, by varying one or more of the reagents. *See* Specification, page 7, lines 14-16. The use of "set" is significant – Webster's defines that term to mean, in relevant part, "a number of things naturally connected by location <set of muscles> <set of footprints> or formation <set of teeth> or order in time <set of temperature readings>". *See* Webster's Third New International Dictionary, page 2087, 1993. The applicant submits that, consistent with this ordinary meaning, the combinatorial libraries recited in the present claims are "sets" or aggregations of compounds related by location and preparation, and not merely individual compounds in isolation.

The specification's subsequent description of three types of libraries confirms this. First, the specification describes libraries that are prepared "as a large mixture of compounds", in which individual compounds can be identified and distinguished by physical and/or chemical characteristics. *See id.* at page 7, lines 16-22. Next, the specification describes libraries that are prepared as individual compounds identified by their respective positions in an array, which are

prepared by massively parallel synthesis of individual compounds. *Id.*, lines 22-25. Third, the specification describes libraries that are prepared as “a set of sub-pools, each having a known element and a random element”, in which individual compounds are identified by deconvolution. *Id.*, lines 25-36. In each case, the compounds in the library are related by location – whether as members of a common mixture, individual compounds distributed in a common array, or as members distributed in sub-pools – and by preparation, according to the methods described in the specification. Nowhere in the applicant's specification is there any suggestion that combinatorial library can be read more broadly to describe conceptual “collections” of compounds as the Examiner suggests.

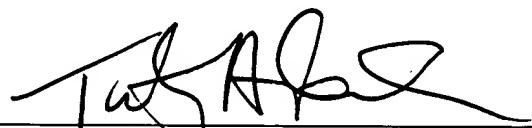
By contrast, as its title and Abstract show, Palfreyman is directed to individual compounds and methods of their use. *See* Palfreyman, Title (“Compounds and Methods for Treating Depression”); Abstract. While the Examiner repeatedly refers to Palfreyman's “collections of compounds”, there is nothing in the reference that discloses or even suggests that the individual compounds being discussed are related by anything more than their common molecular formula and their conceptual inclusion in a common patent. Because it thus fails to disclose or suggest a “combinatorial library” as the claims require, Palfreyman cannot anticipate or render obvious the present claims.

Enclosed is a \$410 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: \_\_\_\_\_

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Timothy A. Porter  
Reg. No. 41,258

Fish & Richardson P.C.  
500 Arguello Street, Suite 500  
Redwood City, California 94063  
Telephone: (650) 839-5070  
Facsimile: (650) 839-5071